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10/590,927	04/09/2007	Axel Niendorf	5151-21PUS	4186

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EXAMINER
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STRZELECKA, TERESA E

ART UNIT	PAPER NUMBER
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1637

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05/05/2009

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/590,927	<b>Applicant(s)</b> NIENDORF ET AL.	
	<b>Examiner</b> TERESA E. STRZELECKA	<b>Art Unit</b> 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 05 February 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 24-60 is/are pending in the application.
- 4a) Of the above claim(s) 29,30,33-35,42,43,46,48,52,53 and 55-58 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 24-28,31,32,36-41,44,45,47,49-51,54,59 and 60 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |                                                                                        |                                                                   |
|----------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>8/28/06;1/25/07;4/9/07</u> .                                  | 6) <input type="checkbox"/> Other: _____                          |

**DETAILED ACTION*****Election/Restrictions***

1. Applicant's election with traverse of species B, D, F, H and L in the reply filed on February 5, 2009 is acknowledged. The traversal is on the ground(s) that the claims have a common special technical feature since claims 24 or 25 are not anticipated by Erlander et al., since Erlander et al. do not teach an image processing system. This is not found persuasive because Erlander et al. teach image processing system both inherently and specifically. First, they teach histological and cytological examination of cells (page 3, [0023]; page 4, [0025]; page 5, [0034], [0036]). Therefore, as evidenced by the articles cited from Encyclopedia Britannica (downloaded April 30, 2009), both histological and cytological examination is carried out using at least a microscope, i.e., an image processing system. Erlander et al. also specifically teach an image processing system (page 7, [0064]):

"Methods for collecting cytological specimens for use in the present invention are known in the art and have been described herein. In the case of breast cancer, such specimens include fine needle aspirates and ductal lavage which can be used to prepare cytological smears or a ThinPrep®. These may then be reviewed by a cytologist or image analysis to identify cells of interest for which additional information is desirable. Cells of this type are typically those identified as a typical, suspicious or malignant, although benign cells may also be isolated for subtype analysis."

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 29, 30, 33-35, 42, 43, 46, 48, 52, 53 and 55-58 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on February 5, 2009.

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3. Claims 24-28, 31, 32, 36-41, 44, 45, 47, 49-51, 54, 59 and 60 will be examined.

***Information Disclosure Statement***

4. The information disclosure statement (IDS) submitted on August 26, 2008 is in compliance with the provisions of 37 CFR 1.97 with the exception of the first three non-patent literature documents, which have not been provided. Accordingly, the information disclosure statement is being considered by the examiner except for these three documents.

5. The information disclosure statements (IDSs) submitted on January 25, 2007 and April 9, 2007 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

***Priority***

6. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Germany on February 26, 2004. It is noted, however, that applicant has not filed a certified copy of the foreign priority application as required by 35 U.S.C. 119(b).

Therefore the priority date of the instant claims is February 25, 2005, the filing date of the PCT application.

***Claim Interpretation***

7. Applicants defined the term "non-morphological analytical testing" in paragraph [0017] as follows:

"In the discussion which follows, the term "nonmorphological analytical testing" is understood to mean especially molecular-biological analyses."

8. Applicants did not define the term "image processing system", therefore it is interpreted as any device or system used in visualizing samples or cells, such as a microscope, for example.

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9. The phrase " wherein the determined at least one of a quantitative fraction of diseased tissue or cells and another morphological aspect is used as a reference quantity on which evaluation of a result of the non-morphological analytical testing is based" is interpreted as any correlation between morphological aspects and results of non-morphological analytical testing, since the term "reference quantity" was not defined.

***Claim Rejections - 35 USC § 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 24-28, 31, 32, 38-41, 44, 45, 47, 49-51 and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by Erlander et al. (US 2003/0186248 A1; cited in the IDS and in the previous office action).

Claims 24 and 25 will be considered together in claim 24, since it is a species of claim 25.

Regarding claims 24 and 25, Erlander et al. teach a method comprising:

preparing sections from the tissue sample (page 3, [0020], [0022]; page 13, [0130]);

subjecting at least one portion of the sample to a histological/cytological examination (page 3, [0023]; page 4, [0025]; page 13, [0131]); and

subjecting at least another portion of the sample to a non-morphological analytical testing (page 3, [0024]; page 4, [0028]; page 13, [0132]),

wherein in the histological/cytological examination, at least one of a quantitative fraction of diseased tissue or cells and another morphological aspect of the at least one portion of the sample is determined by an image processing system (page 4, [0025]; page 6, [0039]; page 7, [0064]; page 13,

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[0131]; since the histological or cytological examination is performed using a microscope, as evidenced by Encyclopedia Britannica, Erlander et al. inherently teach using an image processing system), and

wherein the determined at least one of a quantitative fraction of diseased tissue or cells and another morphological aspect is used as a reference quantity on which evaluation of a result of the non-morphological analytical testing is based (page 3, [0022] and [0024]; page 5, [0034]-[0036]).

Regarding claim 26, Erlander et al. teach fine needle aspiration and scraper sampling (page 3, [0020]).

Regarding claims 27 and 28, Erlander et al. teach that morphological appearance of the cells is correlated with the expression pattern of the genes (page 3, [0022], [0024]; page 4, [0025]-[0030]).

Regarding claims 31 and 32, Erlander et al. teach frozen samples (page 13, [0130]).

Regarding claims 38 and 39, Erlander et al. teach using the results for experimental pathological analysis (page 3, [0022], [0024]; page 4, [0025]; [0026]).

Regarding claims 40 and 41, Erlander et al. teach detecting biomolecules such as DNA, mRNA (page 4, [0028]).

Regarding claims 44 and 45, Erlander et al. teach using microarrays (page 8, [0069], [0077]; page 10, [0094]; page 11, [0102], [0103]; page 13, [0121]-[0128]).

Regarding claims 47 and 49, Erlander et al. teach amplification (page 8, [0075]; page 10, [0100]; page 12, [0111]; page 13, [0132]).

Regarding claims 50 and 51, Erlander et al. teach staining (page 9, [0088]; page 13, [0130]).

Regarding claim 54, Erlander et al. teach subjecting cells to additional staining (page 7, [0065]).

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12. Claims 24, 25, 27, 28, 31, 32, 38-41, 44, 45, 47, 49-51 and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by Adeyinka et al. (Clin. Cancer Res., vol. 8, pp. 3788-3795, 2002).

Claims 24 and 25 will be considered together in claim 24, since it is a species of claim 25.

Regarding claims 24 and 25, Adeyinka et al. teach a method comprising:

preparing sections from the tissue sample (page 3789, second and third paragraph);

subjecting at least one portion of the sample to a histological/cytological examination (page 3789, third paragraph); and

subjecting at least another portion of the sample to a non-morphological analytical testing (page 3789, paragraphs 4 and 5; page 3790, paragraphs 2-4),

wherein in the histological/cytological examination, at least one of a quantitative fraction of diseased tissue or cells and another morphological aspect of the at least one portion of the sample is determined by an image processing system (page 3789, second paragraph; since the histological examination is performed using a microscope, as evidenced by Encyclopedia Britannica, Adeyinka et al. inherently teach using an image processing system), and

wherein the determined at least one of a quantitative fraction of diseased tissue or cells and another morphological aspect is used as a reference quantity on which evaluation of a result of the non-morphological analytical testing is based (page 3791, paragraphs 2-4; Table 2; Fig. 2; page 3792, last paragraph; page 3793, paragraphs 1-3).

Regarding claims 27 and 28, Adeyinka et al. teach that morphological appearance of the cells is correlated with the expression pattern of the genes (page 3791, paragraphs 2-4; Table 2; Fig. 2; page 3792, last paragraph; page 3793, paragraphs 1-3).

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Regarding claims 31 and 32, Adeyinka et al. teach frozen samples (page 3789, second paragraph).

Regarding claims 38 and 39, Adeyinka et al. teach using the results for experimental pathological analysis (page 3791, paragraphs 2-4; Table 2; Fig. 2; page 3792, last paragraph; page 3793, paragraphs 1-3).

Regarding claims 40 and 41, Adeyinka et al. teach detecting biomolecules such as mRNA (page 3789, paragraphs 4 and 5; page 3790, paragraphs 2-4).

Regarding claims 44 and 45, Adeyinka et al. teach using microarrays (page 3790, second paragraph).

Regarding claims 47 and 49, Adeyinka et al. teach amplification (page 3790, third and fourth paragraphs).

Regarding claims 50 and 51, Adeyinka et al. teach staining (page 3789, second paragraph).

Regarding claim 54, Adeyinka et al. teach subjecting cells to additional histological examination (page 3789, third paragraph).

### ***Claim Rejections - 35 USC § 103***

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

14. Claims 59 and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Erlander et al. (US 2003/0186248 A1; cited in the IDS and in the previous office action).

Claims 59 and 60 are drawn to the methods of claims 24 and 25 used to adjust patient's individualized cancer therapy. Erlander et al. teach the methods of claims 24 and 25. In addition,



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they teach that the results of correlation between histological/cytological features and sensitivity or resistance to a particular therapeutic agent or treatment, including information regarding the likelihood of success or failure of various treatment regimens for the disease (page 4, [0026]).

Therefore, in view of these teachings of Erlander et al., it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the information regarding treatment outcomes to adjust therapy of individual patients based on their histological and molecular signatures.

15. Claims 36 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adeyinka et al. (Clin. Cancer Res., vol. 8, pp. 3788-3795, 2002) and Sgroi et al. (Cancer Res., vol. 59, pp. 5656-5661, 1999).

A) Regarding claims 36 and 37, Adeyinka et al. teach preparing the sections for non-morphological analysis from frozen tissue blocks which are mirror-images of formalin-fixed tissue blocks (page 3789, first paragraph), but do not teach using tissue sections adjacent to sections used for non-morphological testing for histological/cytological examination.

B) Sgroi et al. teach analysis of tissue sections from a breast cancer using histology and microarray hybridization (page 5656, paragraphs 3-5; page 5657, paragraphs 1-3). They teach confirmation of the array analysis data by analyzing sections adjacent to the ones used for microarray analysis by immunohistochemistry (page 5657, fifth paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the additional confirmation method of Sgroi et al. in the method of Adeyinka et al. The motivation to do so is provided by Sgroi et al., who state (page 5659, last paragraph; page 5660, first paragraph):

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"As an additional means to confirm our data at the protein level, we performed immunohistochemical analysis of apolipoprotein using tissue sections that were adjacent to those used for laser microdissection. Paralleling the differential expression pattern observed with the cDNA microarray and RTQ-PCR analysis, the invasive cells demonstrated abundant and strong immunoreactivity for apolipoprotein D, whereas the metastatic cells demonstrated rare and weak immunoreactivity (Fig. 3B). This result further supports the reliability of our expression data and demonstrates the cellular specificity of the apolipoprotein gene expression. Overall, the RTQ-PCR and immunohistochemistry results support the feasibility of our microarray experimental protocol as a means to assess *in vivo* transcript expression profiles."

16. No claims are allowed.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA E. STRZELECKA whose telephone number is (571)272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Teresa E Strzelecka  
Primary Examiner  
Art Unit 1637

/Teresa E Strzelecka/  
Primary Examiner, Art Unit 1637  
May 1, 2009